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August 14, 2002

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Application No.	:	**2,352,515**
Owner	:	COMBINATORX, INCORPORATED
Title	:	**METHODS FOR IDENTIFYING COMBINATIONS OF ENTITIES AS THERAPEUTICS**
Classification	:	C12Q-1/02
Your File No.	:	**502-175**
Examiner	:	Nicole Harris

IN ACCORDANCE WITH SUBSECTION 30(2) OF THE PATENT RULES, YOU ARE HEREBY NOTIFIED OF A REQUISITION BY THE EXAMINER. IN ORDER TO AVOID ABANDONMENT UNDER PARAGRAPH 73(1)(A) OF THE PATENT ACT, A WRITTEN REPLY MUST BE RECEIVED WITHIN 6 MONTHS AFTER THE ABOVE DATE.

This application has been examined as amended on April 2, 2002.

The number of claims in this application is 63.

A search of the prior art has revealed the following:

References Applied:

Canadian Patent

2290505	November 19, 1998	Stylli et al.

Publications

Drug Discov Today 4(8):363-369	Aug. 1999	Mere et al.
Chem Biol 6(2):71-83	February 1999	Stockwell et al.
Oncogene 18(23):3546-52	June 10, 1999	Huang et al.

Stylli et al. disclose a robotic system and method of use for rapidly screening at least one chemical combinatorial library for useful molecules using biochemical or cell based arrays. The activity of the molecules is quantified by fluorescent means and the robotic method allows for rapid screening of up to 25,000 chemicals in a 24 hour period.

Mere et al. disclose an automated micro-fluidic system for screening up to 100,000 compounds using biochemical or cell based arrays in a 3456 (48 x 72) well format. Activity of the compounds is quantified using fluorescent resonance energy transfer (FRET).

Stockwell et al. discloses a cell-based assay, termed a cytoblot, for the high-throughput screening of small molecule libraries. The method uses cells seeded in a 384,1536 or 6144 well format, incubation with the molecules of interest, and quantification of interacters by antibodies or chemilluminescence.

Huang et al. disclose a method for determining the profile of mRNA expression in cancer cells. The method involves subtractive hybridization of a cancer cell cDNA library with a control cell cDNA library, the formation of a subtractive cDNA array, the hybridization of the cDNA array with fluorescent labeled cancer cell mRNA or fluorescent labeled control cell mRNA and quantification of the fluorescent signal to determine mRNA expression patterns.

The examiner has identified the following defects in the application:

Claims 1, 26-28, 46-48, 60 and 61 do not comply with Paragraph 28.2(1)(b) of the Patent Act because these claims include subject matter disclosed in Stylli et al. before the claim date. The robotic method of Stylli et al. which screens at least one chemical library using biochemical or cell based arrays, and the compounds identified by said method anticipates and is encompassed by the methods and combinations of entities of these claims.

Claims 1, 26-28, 46-48, 60 and 61 do not comply with Paragraph 28.2(1)(b) of the Patent Act because these claims include subject matter disclosed in Mere et al. before the claim date. The automated method of Mere et al., for screening libraries of compounds in 3456 well arrays, and the compounds identified by said method anticipates and is encompassed by the methods and combinations of entities of these claims.

Claims 1, 26-28, 46-47, 60 and 61 do not comply with Paragraph 28.2(1)(b) of the Patent Act because these claims include subject matter disclosed in Stockwell et al. before the claim date. Stockwell et al. discloses a method for screening combinations of combinatorial library compounds in 384, 1536 or 6144 well arrays. The method of Stockwell et al. and the compounds identified using said method anticipates and is encompassed by the methods and combinations of entities of these claims.

Claims 1, 26-28, 46-47 and 61 do not comply with Paragraph 28.2(1)(b) of the Patent Act because these claims include subject matter disclosed in Huang et al. before the claim date. Huang et al. discloses a cDNA array made from the subtractive hybridization of a treated cancer cell cDNA library and an untreated cancer cell cDNA. The fluorescent labeled mRNA

from various cell sources is used to probe the cDNA array to determine mRNA expression patterns in the cancer cells. The methods of Huang et al. and the mRNA identified by said methods anticipates and is encompassed by these claims.

Claims 1, 28, 48 and 60-62 are ambiguous and do not comply with Subsection 27(4) of the Patent Act. There is no relationship between the individual steps of the methods. These methods merely recite a theoretical approach for screening large quantities of molecules. The example on page 34 of the disclosure describes the invention as a method for screening a number of different compounds (7) in all possible pair-wise combinations (21), in a micro-array format, to identify combinations of compounds with a specific function. However, the language of these claims is so broad it fails to specifically describe the invention. The terminology used in these claims is confusing and uses vague undefined terms such as "entity", "higher order" , "entities", "distinct biological moieties", "test element", "entity/test element", and "combinations of entities". The double use of the term "entity" in the phrasing of "screening....entity" and "at least....entities" is especially unclear. The steps of these methods need to be defined in clear and unambiguous language.

Claims 25 and 45 are directed to a method of medical treatment which is outside the definition of invention in Section 2 of the Patent Act. (See Tennessee Eastman v Commissioner of Patents (1974) S.C.R. 111).

Claims 26, 27, 46 and 47 are outside the definition of invention in Section 2 of the Patent Act. These claims include subject matter that is old and known. The combination of entities claimed in claim 26 and 46 include any chemical combinatorial library that is currently in existence. There is nothing new in preparing the pharmaceuticals of claims 27 and 47 by simply adding a carrier to an old and known compound.

Claims 27 and 47 do not comply with Subsection 27(4) of the Patent Act for not fully and explicitly defining a composition in terms of its constituent elements and their relative amounts. Further, a composition claimed must be fully disclosed, novel and useful.

Claim 61 is indefinite and do not comply with Subsection 27(4) of the Patent Act. The term "the identified entities" has no antecedent.

This application does not comply with Subsection 27(3) of the Patent Act. The specification does not correctly and fully describe the invention and its operation or use. Figure 4 attempts to summarize the steps of the method for performing combinatorial screening. However, there is no relationship between the individual components of the method. Further, the description of figure 3 on pages 11 and 31 refers to rows A-P however, the plates of figure 3 contain rows A-N.

The table that appears on page 36 requires a table number and title. Reference to said table in the description should be made using said reference number.

The last line that appears on page 37 should be removed or moved to the first page of the claims.

The term "NFAT" on page 17 should be defined in words.

Under Section 76 of the Patent Rules, every trade-mark must be identified as a trade-mark. If "premarin" on page 4; "tween" on page 15; "triton-x" on page 17; "multidrop" on page 19; "hydra" on page 25; "ivek digispense" on page 26; "omni" on page 29; "microsoft" on page 30; "ecl" and "analyst AD" on page 34 are trade-marks, they must be so identified.

A statement in an application, such as found on page 21, line 2 and page 37, which incorporates by reference any other document, does not comply with Subsection 81(1) of the Patent Rules.

In accordance with Subsection 81(2) of the Patent Rules, all documents referred to in the description of an application must be available to the public. Hyperlink references are not acceptable references since the links are not static may change over time. References to the hyper links on pages 10, 20 and 26 must be deleted.

Under Section 29 of the Patent Rules, applicant is requisitioned to provide particulars of the prior art cited in the prosecution of the corresponding United States and European Patent Office applications and the patent numbers. If the particulars are not available to the applicant, the reason why must be stated.

In order to assist the prosecution of this application, applicant is requisitioned to provide a copy of all non-patent citations.

In view of the foregoing defects, the applicant is requisitioned to amend the application in order to comply with the Patent Act and the Patent Rules or to provide arguments as to why the application does comply.

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